NIEHS, National Toxicology Program
NIOSH, Industrywide Studies Branch
Interagency Agreement

Update on Current Collaborative Research

Elizabeth Whelan

December 15, 2016

NTP and NIOSH: Common Goals

- To provide scientific data and knowledge necessary for making appropriate decisions that protect and improve public health.

- Establish and maintain partnerships with other federal agencies to leverage resources and reduce undue overlap

Goals of the NTP/NIOSH Collaboration

- Conduct exposure and health assessments of priority agents of mutual interest to NTP and NIOSH
- Capitalize on NIOSH access to human populations and work sites to provide real-world context for toxicology studies
- Guide decision-making for NIOSH epidemiologic studies
- Toxicology and epidemiology studies provide evidence-base for guidance documents
  - Report on Carcinogens, OHAT reviews, NIOSH Criteria Documents

Impact of the Collaboration

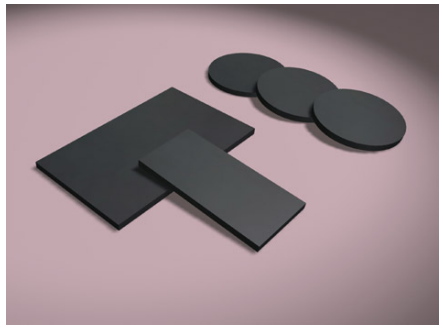
- Findings inform testing priorities
- Guides selection of relevant laboratory test exposures and doses (e.g., CNT)
- Has led to development of methods for generation of laboratory test exposures (e.g., welding fume, asphalt fume)

Update of Current Studies

- Indium
- Manganese Fractions In Welding Fume
- Carbon Nanotubes and Carbon Nanofibers
- Bisphenol A
- PAHs in Coal Tar Sealant Applications
- Flame Retardants
- 1-Bromopropane

Use of and Occupational Exposure to Indium in the United States

Cynthia J. Hines, MS, CIH, FAIHA
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention



Background

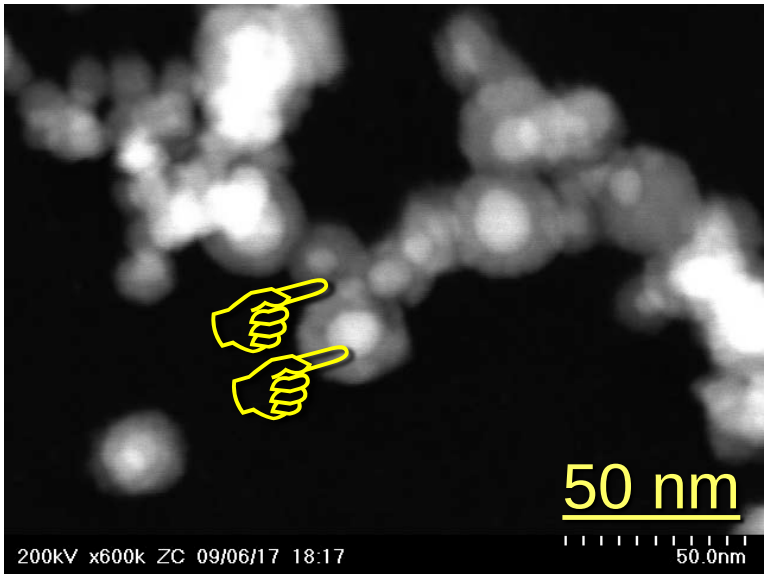
- Indium
  - A metal with limited use historically; however, use of indium tin oxide (ITO) in flat panel displays has increased substantially over the past decade
- Toxicity
  - ITO exposure associated with lung disease in Asian and U.S. workers
  - Similar lung effects seen in animals in the 1960s for related indium compounds
  - Toxicity appears to vary by type of indium compound
  - Indium appears to persist in the body (i.e. eliminated slowly)
- Data Gap
  - Little known about indium use in the U.S. and worker exposure levels
- NIOSH Study
  - Contacted a range of companies to obtain information about indium use
  - Requested indium air sampling data, if available
  - Conducted site visits and collected air samples at selected companies

Findings

- U.S. Uses
  - solder (most common)
  - thin film of ITO
  - indium phosphide (InP) in semiconductor fabrication
  - some photovoltaic cells
  - sputter target manufacturing (as ITO or metal alloys)
  - some alkaline batteries
- Elevated Indium Exposure
  - Tasks involving mechanical abrasion of ITO
  - Handling indium salts and powders
  - Some indium air concentrations exceeded the NIOSH REL & ACGIH TLV
- Minimal Indium Exposure
  - Processes where indium remained a molten metal
  - Processing InP semiconductor substrates (due to engineering controls for preventing phosphine exposure)
  - Alkaline battery manufacturing

Hines CJ, Roberts JL, Andrews RN et al (2013). Use of and occupational exposure to indium in the United States. *J Occup Environ Hyg* 10:723-733.

Occupational Exposure Assessment Of Manganese Fractions In Welding Fume



Kevin W. Hanley, MSPH, CIH, REHS/RS

National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention

Occupational Exposure Assessment Of Manganese Fractions In Welding Fume

- Objective: to characterize welders' exposures to 4 manganese fractions based on chemical solubility of different Mn oxidation states

- NIOSH evaluated novel method for soluble Mn; Mn (0, 2+); Mn (3+, 4+); insoluble Mn; (& Mn-sum)
- Conducted 10 monitoring surveys: Construction at oil refineries; shipyard; steel fabricators; heavy equipment & appliance mfg

- Over 300 full-shift worker-day breathing zone TWA measurements were collected (required > 650 samples; x5 analytes = ~3250 data pts.)

Occupational Exposure Assessment Of Manganese Fractions In Welding Fume

- Manuscript published, *J Occ & Environ Hyg (2015)*
  - Refinery construction, SMAW (stick welding)
  - GM Mn-sum levels ranged 5.7 – 210 $\mu g/m^3$
  - Welders' exposures > ACGIH TLV, total Mn
  - > 10x ACGIH TLV, respirable – confined space

- Manuscript accepted for January 2017 publication,

  Annals Work Exp & Health
  - Heavy equipment – GMAW (MIG welding)

- Mn 0,2+ and Mn 3+,4+ most abundant (~85% of Mn-sum)
- Evaluated method for Mn sequential extraction
  - NIOSH Method draft 7305 & manuscript published, *Analytical Chem (2015)*

Industrywide Exposure Assessment Study of Workers Exposed to Carbon Nanotubes and Carbon Nanofibers

Matthew Dahm, MPH
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention

Carbon Nanotubes (CNT) Exposure Assessment, NTP Funding FY12 – FY14

- **Objective:** conduct exposure assessments for carbon nanotubes and carbon nanofibers (CNT/CNF) in a representative sample of US workplaces.

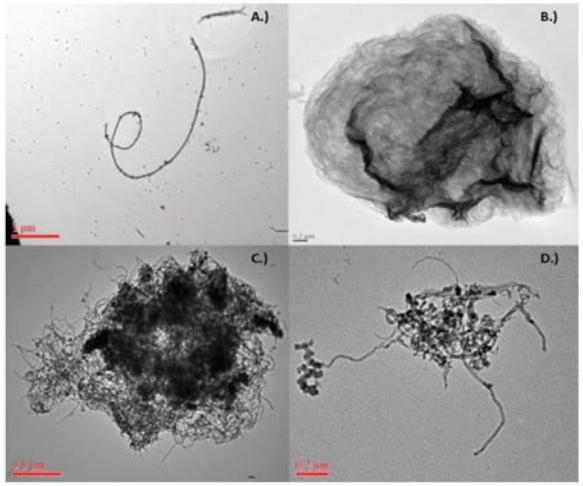
- **Conducted 19 Site Visits (12 with cross-sectional epi study)**
  - CNT/CNF Primary Manufacturers
  - CNT/CNF Secondary Manufacturers (Electronics and Composites Facilities)
    - 128 Workers Sampled (2 days each)
      - 480 Full Shift, Personal Respirable and Inhalable Elemental Carbon Samples
      - 256 Full Shift, Personal Samples analyzed by TEM
      - ~ 105 Dermal Samples (analyzed by SEM)
      - ~ 90 Sputum Samples (analyzed by hyperspectral imaging)

- **Overall Personal Exposures (from 12 most recent site visits)**
  - Respirable- mean 1.0 µg/m^3 (median 0.10 µg/m^3)
  - NIOSH Recommended Exposure Limit (REL) = 1 µg/m^3 (exceeded by 7% of workers)
  - Inhalable- mean 6.2 µg/m^3 (median 0.24 µg/m^3)

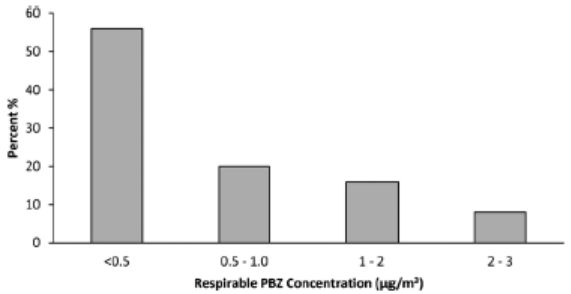
CNT Exposure Assessment Project

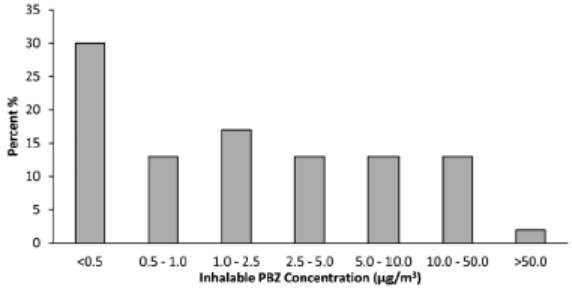
Results from Dahm et al. Ann Occup Hyg., 2015

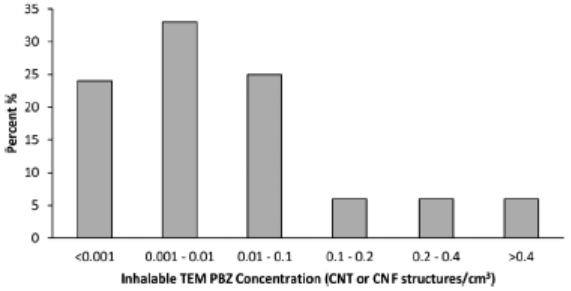
Few single fibers



- Most respirable exposures well below the NIOSH REL
- Much higher inhalable exposures (unclear toxicological implications)
- TEM structure concentrations exhibited more sensitivity to detection (but more costly—and no REL)
- Most agglomerate structures were in the 2-5 or 5-10 µm size class







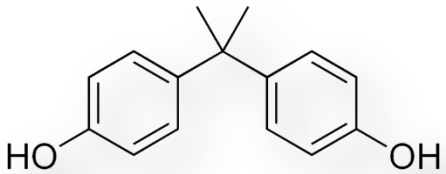
Carbon Nanotube Feasibility Study

NTP Funding FY12-14

- **Impact**
  - 2014 IARC meeting evaluated CNT carcinogenicity
  - Nordic Expert Group for Criteria Documentation of Health Risks to develop OELs
  - Dahm et al. 2015 received NIOSH Alice Hamilton Award in 2016 for best exposure assessment paper
  - NTP selected a MWCNT for tox testing based on MWCNT types found in Dahm study
- **Publications:**
  - Schubauer-Berigan et al. Characterizing adoption of precautionary risk management guidance for nanomaterials, an emerging occupational hazard. *J Occup Environ Hyg* 2014, DOI: 10.1080/15459624.2014.946515 (3 citations in literature)
  - Dahm MM, et al. Carbon Nanotube and Nanofiber Exposure Assessments: An Analysis of 14 Site Visits. *Ann Occup Hyg., 2015, doi:10.1093/annhyg/mev020* (22 citations in literature)

Urinary Bisphenol A Concentrations Among Manufacturing Workers in the United States

Cynthia J. Hines, MS, CIH, FAIHA
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention



Background

- BPA
  - Used in making polycarbonate, epoxy and phenolic resins, in certain foundry casting waxes, and in thermal paper (largely discontinued)
- Metabolism and Toxicity
  - After ingestion, BPA is rapidly conjugated in the liver and excreted into the urine
  - BPA is considered weakly estrogenic
  - A cross-sectional study of BPA-exposed manufacturing workers in China reported decrements in male sexual function in several domains
- Data Gap
  - Absence of published data on BPA exposure among U.S. manufacturing workers.
- NIOSH Study
  - Recruited 78 workers at 6 companies making or using BPA
  - Collected seven, timed spot urine samples over two consecutive days
  - Measured both free (unconjugated) and total BPA (free + conjugated)
  - Collected information on non-occupational BPA sources & exposure modifiers

Findings

- Total BPA Concentrations
  - Clear evidence of occupational exposure
  - Total BPA increased during work on both days
  - Total BPA, on average, was ~70 times higher than adults in NHANES 2013-2014
- Determinants of Increased BPA Exposure
  - Handling sacks, bags etc. of raw BPA
  - Taking process samples containing BPA
  - Increased body mass index
  - Time point (when sample collected, i.e. higher at end-shift than pre-shift)
  - Job: Highest: working with molten BPA-filled wax; Lowest: flaking phenolic resins
- Other Findings
  - Any dietary BPA exposure was overshadowed by occupational exposure
  - Suggestion that BPA elimination in workers was slower than in oral dosing studies
  - Total BPA concentrations were comparable to those reported in Chinese workers

Hines CJ, Jackson MV, Deddens JA et al (in press). Urinary Bisphenol A (BPA) concentrations among workers in industries that manufacture and use BPA in the United States. Annals of Occupational Hygiene.

Assessment of Exposure to Polycyclic Aromatic Hydrocarbons in Coal Tar Sealant Applicators

Kevin W. Hanley, MSPH, CIH, REHS/RS

National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention

Assessment of Exposure to Polycyclic Aromatic Hydrocarbons in Coal Tar Sealant Applicators

- Coal tar (CT); CT Distillates; CT Pitch – complex mixtures, variable PAH composition and concentrations
- "refined" Coal Tar Sealants ("RTS"; RT12) – blended emulsion using 30-35% processed CT pitch in water, clay & sand
- Known human carcinogens – NTP, IARC, ACGIH, NIOSH
  - Except refined-Coal Tar Sealants – *No Data*
- US Geological Survey research publications have reported PAHs in CTS products, nearby streams, flaked debris, & house dust
- Bans - Cities, states, water basins, universities & hardware stores
- Pavement Coating Technology Council (PCTC) contends that CT-based sealants are safe and lobby against CTS bans
- US EPA settled a lawsuit regarding industrial storm water run-off

CDC NIOSH

Assessment of Exposure to Polycyclic Aromatic Hydrocarbons in Coal Tar Sealant Applicators

- Two site surveys conducted during pavement sealant jobs in FY16; six more expected in FY17
- Pavement sealing tasks & concurrent PAH exposures:
  - Vehicles; gas blowers & generators; asphalt crack fill
  - Apply CT sealant: manually; spraying or vehicles for large areas
- Exposures will be measured by breathing zone air, skin wipes, and metabolites in pre/post-shift urine & blood
- Air samples and skin wipes will be analyzed for 16 PAHs & 4 N-heterocyclics; BSF - limited
- Urine specimens will be analyzed for 1–hydroxypyrene; 1- & 2-Hydroxynaphthalene; total OH-PAH metabolites; cotinine; creatinine

CDC NIOSH

U.S. PUBLIC HEALTH SERVICE 1798

Assessment of Occupational Exposure to Flame Retardants

Cheryl F. Estill, PhD

Widely added to U.S. products; changing rapidly due to polybrominated diphyenyl ethers (PBDEs) phase-out

<u>Flame Retardants</u>

- tetrabromobisphone A (TBBPA)
- 2,3,4,5 – tetrabromobenzoate (TBB)
- 2,3,4,5 – tetrabromophthalate (TBPH)
- decabromodiphenyl ethane (DBDPE)
- hexabromocyclododecane (HBCD)
- tris (1,3-dichloro-2-propyl) phosphate (TDCPP)
- tris (1-chloro-2-propyl) phosphate, (TCPP)
- tricresyl phosphate(TCP)
- triphenyl phosphate (TPP)

Assessment of Occupational Exposure to Flame Retardants

Methods

- Characterize exposures in various industries:
  - spray polyurethane foam
  - nail salons
  - manufacture and installation of insulation
  - manufacture of automotive interiors
  - gymnasiums
  - manufacture of carpet padding
  - fire service
- Collect exposure information from workers over two days
- Samples to Collect:
  - urine
  - serum
  - air
  - hand wipe
  - bulk of product being used

Assessment of Occupational Exposure to Flame Retardants

Current Status

- Conducting year three of data collection
- Collected data from 14 workplaces
- Enrolled 106 workers in the study
- Samples are being analyzed

Occupational Exposure to 1-Bromopropane

- NTP-funded studies (2003-2006) contributed to13th Report on Carcinogens
- NIOSH participated this year in IARC Monograph 115 where 1-BP classified as 2B
- NIOSH Criteria Document – public meeting this year
- EPA, ATSDR draft assessments
- ACGIH TLV lowered from 10 ppm to 0.1 ppm

Thank You
Questions?